

## REMARKS

The amendment to the specification is made to add claims that are the same or substantially the same as claims as found in third party patent application publications, namely in 20050037392, 20050042648, 20050079510, 20050130173, and 20040185484.

The chart below shows each claim and support therefore in the specification. It also identifies the claim in a third party application that it is the same or substantially the same as.

Additional claim fees are believed due in connection with this paper. The Director is authorized to debit our deposit account no. 19-0733 in the appropriate amount. Applicants respectfully solicit favorable consideration and allowance of the instant application. If there are any questions, the Examiner is invited to contact the undersigned to further prosecution.

NEW CLAIM	SUPPORT	PUBLISHED APPLICATION SOURCE
<p>64. (New) A method for amplifying a nucleic acid molecule comprising the steps of: (a) forming aqueous compartments in a water-in-oil emulsion, wherein a plurality of compartments include a nucleic acid molecule, a bead capable of being linked to the nucleic acid molecule, and an aqueous solution comprising components necessary to perform nucleic acid amplification; (b) amplifying the nucleic acid molecule in the compartments to form amplified product copies of the nucleic acid molecule; and (c) capturing the amplified product copies to the bead in the compartments, thereby amplifying of the nucleic acid molecule.</p>	<p>“Microemulsions comprising one or more species of analyte DNA molecules are formed. The analyte DNA molecules in the microemulsions are amplified in the presence of reagent beads which are bound to a plurality of molecules of a primer for amplifying the analyte DNA molecules.” ¶10; “The microemulsions are temperature cycled as in a conventional PCR. If a DNA template and a bead are present together in a single aqueous compartment, the bead bound oligonucleotides act as primers for amplification.” ¶15, step 3; “Each of the plurality of beads comprises a plurality of bound polynucleotides. ” ¶108 “Product beads are formed that are bound to a plurality of copies of a single species of analyte DNA molecule.” ¶10.</p>	<p>20050037392, claim 2</p>
<p>65. (New) The method of claim 64, wherein the nucleic acid amplification is performed using</p>	<p>“For example, for polymerase chain reaction (PCR) the compartments will desirably contain a DNA polymerase</p>	<p>20050037392, claim 4</p>

polymerase chain reaction.	and deoxyribonucleotides.” ¶34	
66. (New) The method of claim 65, wherein the emulsion comprises a detergent.	“The oil phase was composed of 4.5% Span 80 (S6760, Sigma, St. Louis, MO), 0.40 % Tween 80 (Sigma S-8074), and 0.05% Triton X-100 (Sigma T-9284) in mineral oil (Sigma M-3516). ” ¶44; “Detergents which can be used include, but are not limited to Triton X100, Laureth 4, Nonidet.” ¶ 35.	20050037392, claim 6
67. (New) The method of claim 64 wherein the nucleic acid amplification is performed using polymerase chain reaction, and the emulsion is thermostable.	“After PCR cycling, the microemulsion from five wells of a PCR plate were pooled and broken by the addition 800 microliters of NX buffer (100 mM NaCl containing 1% Triton X-100, 10 mM Tris-HCl, pH 7.5, 1 mM EDTA) in a 1.5 ml tube (Corning 430909). ” ¶47	20050037392, claim 15
68. (New) The method of claim 64 wherein the nucleic acid molecule is genomic DNA or cDNA.	“Sample DNA for amplification and analysis according to the present invention can be genomic DNA, cDNA, PCR products of genomic DNA, or PCR products of cDNA, for example.” ¶36	20050037392, claim 16
69. (New) The method of claim 64 wherein a plurality of compartments when formed each contains on average less than one nucleic acid molecule.	“In order to maximize the proportion of beads which are homogeneous with respect to oligonucleotide, it is desirable that on average, each aqueous compartment contains less than 1 template molecule. ” ¶34	20050037392, claim 17

<p>70. (New) A method for amplifying a nucleic acid molecule comprising the steps of: (a) forming aqueous compartments in a water-in-oil emulsion, wherein a plurality of the compartments include a nucleic acid molecule, and an aqueous solution comprising components necessary for nucleic acid amplification; (b) amplifying the nucleic acid molecule in the compartments to form amplified copies of the nucleic acid molecule.</p>	<p>“Microemulsions are made by stirring or agitation of oil, aqueous phase, and detergent. The microemulsions form small aqueous compartments which have an average diameter of 0.5 to 50 microns. The compartments may be from 1 to 10 microns, inclusive, from 11 to 100 microns, inclusive, or about 5 microns, on average. All such compartments need not comprise a bead. Desirably, at least one in 10,000 of said aqueous compartments comprise a bead. Typically from 1/100 to 1/1 or from 1/50 to 1/1 of said aqueous compartments comprise a bead. In order to maximize the proportion of beads which are homogeneous with respect to oligonucleotide, it is desirable that on average, each aqueous compartment contains less than 1 template molecule. Aqueous compartments will also desirably contain whatever reagents and enzymes are necessary to carry out amplification. For example, for polymerase chain reaction (PCR) the compartments will desirably contain a DNA polymerase and deoxyribonucleotides. For rolling circle amplification a DNA polymerase and a generic DNA circle may be present.” ¶34.</p>
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20050042648,  
claim 2

71. (New) The method of claim 70 wherein the nucleic acid amplification is performed using polymerase chain reaction.	For example, for polymerase chain reaction (PCR) the compartments will desirably contain a DNA polymerase and deoxyribonucleotides.” ¶34.	20050042648, claim 5
72. (New) The method of claim 70 wherein the emulsion is thermostable.	“PCR was carried out under the following cycling conditions: 94°C for 2 minutes; 40 cycles of 94°C for 15 seconds, 57°C for 30 seconds, 70°C for 30 seconds.” ¶44; “After PCR cycling, the microemulsion from five wells of a PCR plate were pooled and broken by the addition 800 microliters of NX buffer (100 mM NaCl containing 1% Triton X-100, 10 mM Tris-HCl, pH 7.5, 1 mM EDTA) in a 1.5 ml tube (Corning 430909).” ¶47.	20050042648, claim 11
73. (New) The method of claim 70 wherein the amplified copies of the nucleic acid molecule are linked to a bead.	“Beads, after being prepared according to the present invention as product beads, have more than one copy of the same nucleic acid molecule bound to them.” ¶26.	20050042648, claim 13
74. (New) The method of claim 73 wherein the nucleic acid amplification is performed using polymerase chain reaction, and the emulsion is thermostable.	“PCR was carried out under the following cycling conditions: 94°C for 2 minutes; 40 cycles of 94°C for 15 seconds, 57°C for 30 seconds, 70°C for 30 seconds.” ¶44; “After PCR cycling, the microemulsion from five wells of a PCR plate were pooled and broken by the addition 800 microliters of NX buffer (100 mM NaCl	20050042648, claim 16

	containing 1% Triton X-100, 10 mM Tris-HCl, pH 7.5, 1 mM EDTA) in a 1.5 ml tube (Corning 430909). "¶47.	
75. (New) The method of claim 70 wherein a plurality of compartments when formed each contains on average less than one nucleic acid molecule.	"In order to maximize the proportion of beads which are homogeneous with respect to oligonucleotide, it is desirable that on average, each aqueous compartment contains less than 1 template molecule. "¶34.	20050042648, claim 17
76. (New) A method for amplifying one or more nucleic acids comprising the steps of: (a) forming a water-in-oil emulsion to create a plurality of aqueous compartments wherein at least one of the compartments comprises a single nucleic acid template, a single bead capable of binding to the nucleic acid, and amplification reaction solution containing reagents necessary to perform nucleic acid amplification; (b) amplifying the nucleic acids in the compartments to form amplified copies of said nucleic acids; and (c) binding the amplified copies to the beads in the compartments .	"Microemulsions are made by stirring or agitation of oil, aqueous phase, and detergent. The microemulsions form small aqueous compartments which have an average diameter of 0.5 to 50 microns. The compartments may be from 1 to 10 microns, inclusive, from 11 to 100 microns, inclusive, or about 5 microns, on average. All such compartments need not comprise a bead. Desirably, at least one in 10,000 of said aqueous compartments comprise a bead. Typically from 1/100 to 1/1 or from 1/50 to 1/1 of said aqueous compartments comprise a bead. In order to maximize the proportion of beads which are homogeneous with respect to oligonucleotide, it is desirable that on average, each aqueous compartment contains less than 1 template molecule. Aqueous compartments will also desirably	20050079510, claim 1

	<p>contain whatever reagents and enzymes are necessary to carry out amplification. For example, for polymerase chain reaction (PCR) the compartments will desirably contain a DNA polymerase and deoxyribonucleotides. For rolling circle amplification a DNA polymerase and a generic DNA circle may be present. "¶34;" Beads, after being prepared according to the present invention as product beads, have more than one copy of the same nucleic acid molecule bound to them." ¶26.</p>	
<p>77. The method of claim 76 wherein said emulsion is heat stable.</p>	<p>"PCR was carried out under the following cycling conditions: 94°C for 2 minutes; 40 cycles of 94°C for 15 seconds, 57°C for 30 seconds, 70°C for 30 seconds." ¶44; "After PCR cycling, the microemulsion from five wells of a PCR plate were pooled and broken by the addition 800 microliters of NX buffer (100 mM NaCl containing 1% Triton X-100, 10 mM Tris-HCl, pH 7.5, 1 mM EDTA) in a 1.5 ml tube (Corning 430909)." ¶46.</p>	<p>20050079510, claim 8</p>
<p>78. (New) The method of claim 76, wherein the bead comprises a member of a binding pair and the binding pair is avidin/biotin.</p>	<p>"Beads can be modified by covalent or non-covalent interactions with other materials, either to alter gross surface properties, such as hydrophobicity or hydrophilicity, or to attach molecules that impart binding</p>	<p>20050079510, claim 31</p>

	<p>specificity. Such molecules include without limitation, antibodies, ligands, members of a specific-binding protein pair, receptors, nucleic acids. Specific-binding protein pairs include avidin-biotin, streptavidin-biotin, and Factor VII-Tissue Factor.” ¶25.</p>	
<p>79. (New) A method for sequencing nucleic acids comprising: (a) fragmenting large template nucleic acid molecules to generate a plurality of fragmented nucleic acids; (b) delivering the fragmented nucleic acids into aqueous compartments in a water-in-oil emulsion such that a plurality of aqueous compartments comprise a single copy of a fragmented nucleic acid, a single bead capable of binding to the fragmented nucleic acid, and amplification reaction solution containing reagents necessary to perform nucleic acid amplification; (c) amplifying the fragmented nucleic acids in the compartments to form amplified copies of said nucleic acids</p>	<p>“Beads generated from random fragments of whole genomes (24)” ¶41; “Microemulsions are made by stirring or agitation of oil, aqueous phase, and detergent. The microemulsions form small aqueous compartments which have an average diameter of 0.5 to 50 microns. The compartments may be from 1 to 10 microns, inclusive, from 11 to 100 microns, inclusive, or about 5 microns, on average. All such compartments need not comprise a bead. Desirably, at least one in 10,000 of said aqueous compartments comprise a bead. Typically from 1/100 to 1/1 or from 1/50 to 1/1 of said aqueous compartments comprise a bead. In order to maximize the proportion of beads which are homogeneous with respect to oligonucleotide, it is desirable that on average, each aqueous compartment contains less than 1 template</p>	<p>20050130173, claim 1</p>



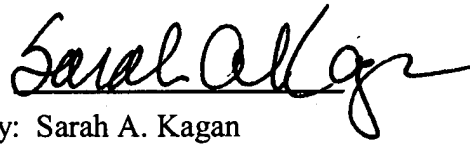
and binding the amplified copies to beads in the compartments ; (d) delivering the beads to an array, and (e) performing a sequencing reaction simultaneously on a plurality of the reaction chambers.	<p>molecule. Aqueous compartments will also desirably contain whatever reagents and enzymes are necessary to carry out amplification. For example, for polymerase chain reaction (PCR) the compartments will desirably contain a DNA polymerase and deoxyribonucleotides. For rolling circle amplification a DNA polymerase and a generic DNA circle may be present.” ¶34, “Template analyte molecules on product beads can be employed for solid phase sequencing. In one solid phase sequencing technique, product beads are arrayed by placing them on slides spotted with complementary oligonucleotides. In another solid phase sequencing technique, product beads are placed into individual wells.” ¶32.</p>	
80. (New) A method for delivering a nucleic acid template to an array, comprising dispersing over the array a plurality of beads, each bead having at least one nucleic acid template immobilized thereon, wherein the nucleic acid template is suitable for use in a nucleic acid sequencing reaction.	<p>“Template analyte molecules on product beads can be employed for solid phase sequencing. In one solid phase sequencing technique, product beads are arrayed by placing them on slides spotted with complementary oligonucleotides. In another solid phase sequencing technique, product beads are placed into individual wells.” ¶32.</p>	20050130173, claim 40

<p>81. (New) A method for sequencing nucleic acids comprising: (a) fragmenting nucleic acid molecules to generate a plurality of fragmented nucleic acids; (b) attaching one strand of a plurality of the fragmented nucleic acids individually to beads to generate single stranded nucleic acids attached individually to beads; (c) delivering a population of the single stranded fragmented nucleic acids attached individually to beads to an array; (d) performing a sequencing reaction simultaneously on a plurality of the reaction chambers.</p>	<p>“Beads generated from random fragments of whole genomes (24)” ¶41; “Beads, after being prepared according to the present invention as product beads, have more than one copy of the same nucleic acid molecule bound to them.” ¶26 “Template analyte molecules on product beads can be employed for solid phase sequencing. In one solid phase sequencing technique, product beads are arrayed by placing them on slides spotted with complementary oligonucleotides. In another solid phase sequencing technique, product beads are placed into individual wells.” ¶32</p>	<p>20050130173, claim 76</p>
<p>82. (New) A method for delivering nucleic acid templates to an array comprising the steps of: (a) providing a population of nucleic acid templates; (b) isolating each nucleic acid template from said population to a bead; (c) delivering a population of said nucleic acid templates isolated to a bead to said array.</p>	<p>“The microemulsions are temperature cycled as in a conventional PCR. If a DNA template and a bead are present together in a single aqueous compartment, the bead bound oligonucleotides act as primers for amplification. The straight red and green lines connected to the beads represent extension products from the two different kinds of templates. ” ¶15; “Template analyte molecules on product beads can be</p>	<p>20040185484, claim 50</p>

	employed for solid phase sequencing. In one solid phase sequencing technique, product beads are arrayed by placing them on slides spotted with complementary oligonucleotides. In another solid phase sequencing technique, product beads are placed into individual wells." ¶32.	
83. (New) The method of claim 81, wherein said isolating step comprises encapsulating said nucleic acid template in an emulsion of a water-in-oil emulsion.	"If a DNA template and a bead are present together in a single aqueous compartment, the bead bound oligonucleotides act as primers for amplification. The straight red and green lines connected to the beads represent extension products from the two different kinds of templates. " ¶15.	20040185484, claim 52
84. (New) The method of claim 81, wherein said nucleic acid template is encapsulated with a bead and wherein the bead can bind said nucleic acid.	If a DNA template and a bead are present together in a single aqueous compartment, the bead bound oligonucleotides act as primers for amplification. The straight red and green lines connected to the beads represent extension products from the two different kinds of templates. " ¶15.	20040185484, claim 53

Respectfully submitted,

Date: 02-17-06

A handwritten signature in black ink, appearing to read "Sarah A. Kagan", written over a horizontal line.

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